Scientists categorize neurons by the way the brain jiggles during a heartbeat

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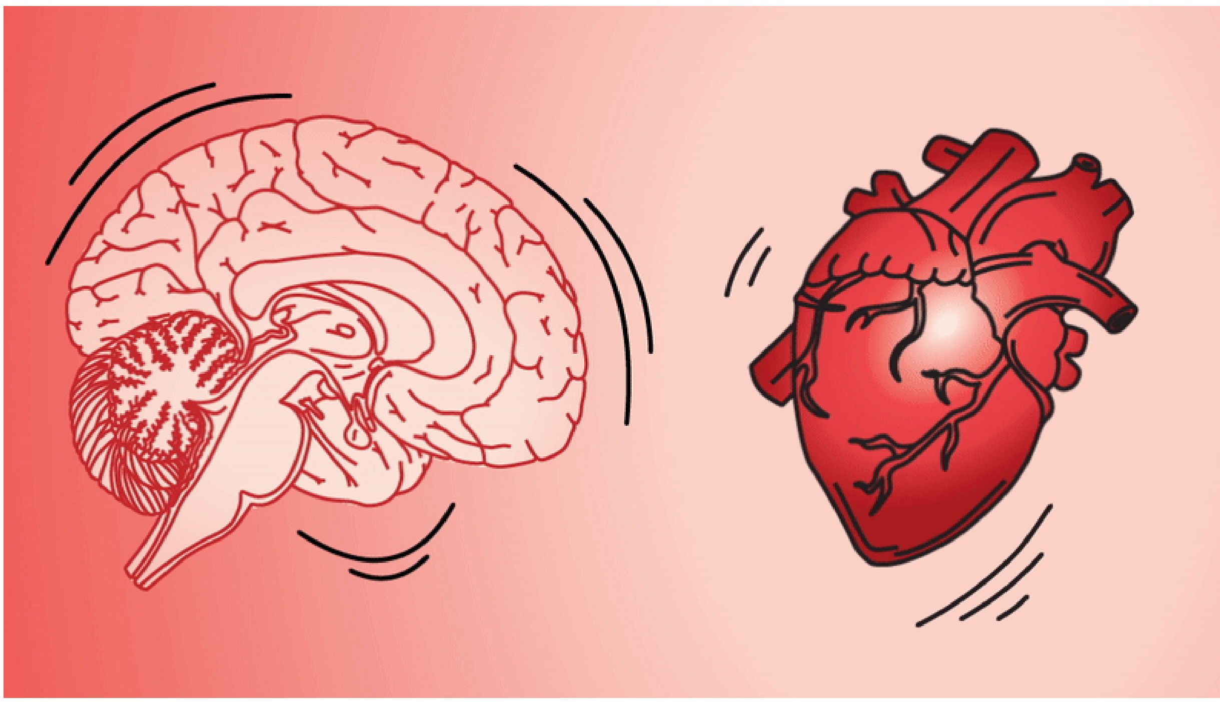


This animation shows how the brain jiggles when the heart beats. Credit: Mosher et al./*Cell Reports*

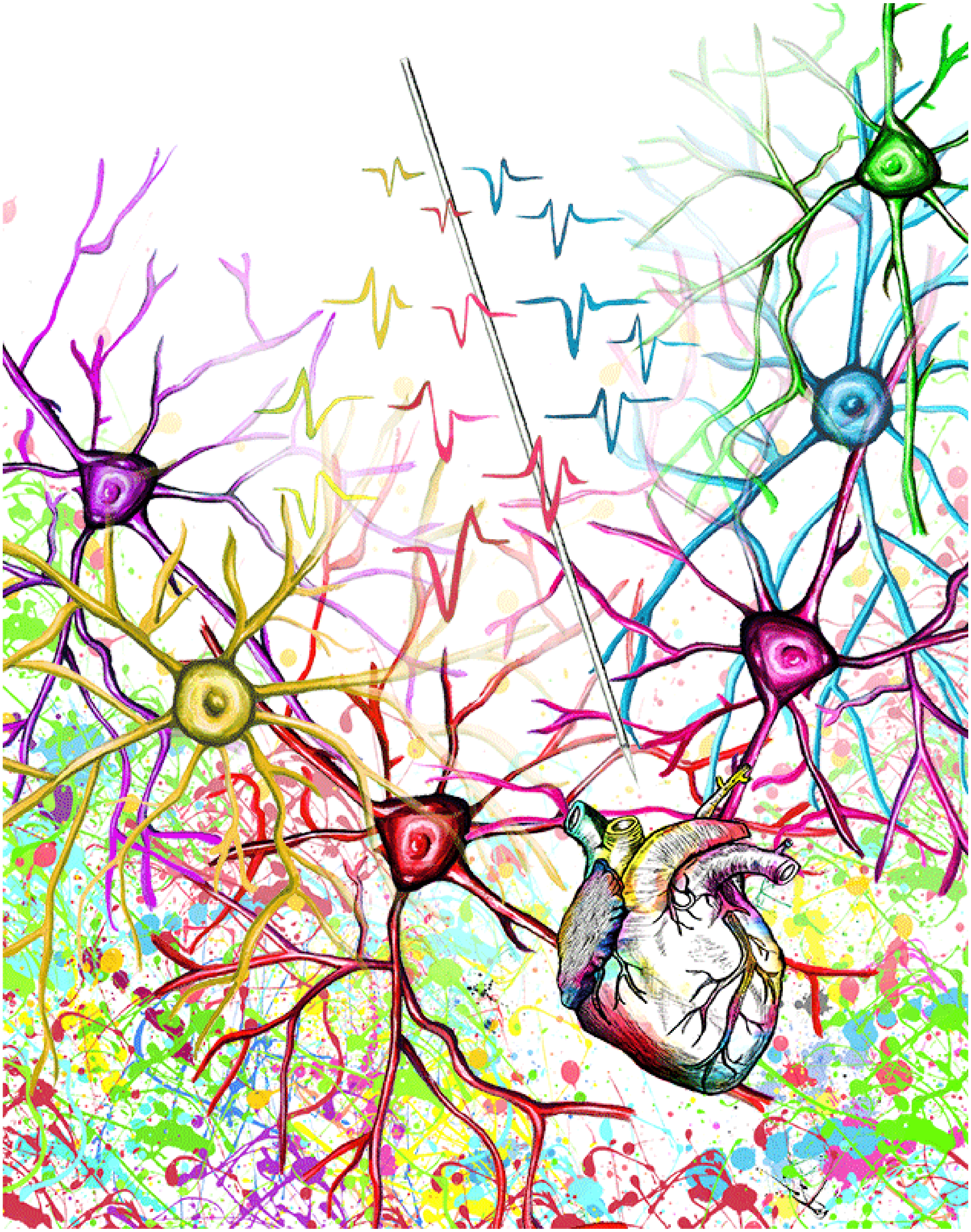
The brain jiggles when the heart beats, and now, researchers have found a way to use that motion to better study the differences between types of neurons. In a study appearing March 10 in the journal *Cell Reports*, researchers find that by analyzing the changes in the waveforms they record from neurons during a heartbeat, they can more accurately classify the different types of neurons in the human brain. This work, they say, could help us better understand how the different types of cells that exist in the brain interact together to produce cognition and behavior.

"We were recording neurons from the brain of human patients implanted with electrodes for neurosurgical procedures, and we lined up the neural activity to the heartbeat and saw that many neurons changed their firing pattern every time the heart beats," says Clayton Mosher, of Cedars-Sinai Medical Center, who is the joint first author of the study with Yina Wei, of the Allen Institute. "We were like, 'Okay. This is surprising,'"

But as the team zoomed in more, they realized that the neurons weren't firing in a different pattern; instead, the brain was jiggling. For every heartbeat, the brain pulses, and the neurons shift their place slightly within the skull. The scientists estimate that the neurons shift about three micrometers, which is less than the width of a hair, during a heartbeat. The appearance of a difference in neuronal firing was created by this movement.

"We started from something that many people viewed as a result of brain motion rather than neural activity. They consider it noisy. They consider it as a limitation of their experiment," says Costas Anastassiou, of the Allen Institute, who is the senior author of the study together with Ueli Rutishauser, of Cedars-Sinai Medical Center. "What we were able to show is that if used it in a smart way, this naturally occurring motion of the brain can tell us much more about the identity of the cells we're recording from. This is because measuring the activity of the same neuron from different locations in the brain provides additional information about the neuron."

Conventionally, scientists classify neurons based on their waveform, a characteristic pattern of electrical activity that each neuron emits every time it becomes active, i.e. when it "spikes." The shape of each neuron's waveform is different. By examining the width of the waveform, scientists can reliably categorize neurons into two types: those with narrow and those with broad waveforms.



This animation illustrates how the waveforms recorded in neurons change when the heart beats. Credit: Mosher et al./*Cell Reports*

Now, the tiny brain motion caused by the heartbeat allows scientists to measure the waveform shape more accurately. As the distance between a neuron and the electrode changes, the measured waveform changes as well. By measuring these changes, the team showed that they can differentiate between three different classes of neurons in the human hippocampus: narrow spike (NS), broad spike one (BS1), and broad spike two (BS2). And each class has different firing properties: the researchers found that BS1 neurons coordinate their activity with gamma waves, whereas BS2 neurons coordinate their activity with theta waves.

"Gamma and theta waves are patterns of activity in the brain that are highly relevant to cognition. We know, for example, that memory and learning are very closely linked with theta oscillations. We know that attention is closely linked with gamma oscillations," says Anastassiou.

"At the end of the day, to understand how the brain works, we need to understand what different types of cells exist in the brain, and how these cell classes interact together to produce cognition and behavior," he says. "One needs to be able to bridge across scales to say how the microscopic world gives rise to this behavioral phenomenon happening in the macroscopic world. Our work reveals, for the first time, how to achieve such a bridge between scales for the human brain."

One of the challenges in neuroscience is that there is often a difference between how neurons behave in living humans and how they behave when investigated in isolation in a brain slice. Through recordings from human brain tissue, the researchers were able to construct single-cell models that simulate the biophysical features and morphology of real neurons. The model bridges the in-vivo brain and ex-vivo brain slice recordings to serve as a novel tool to categorize neurons. The computational models of human neurons can be used to better understand the signals we record from live human beings implanted with electrodes.

"Ultimately, what we want to understand is, one, how different types of neurons in the human brain contribute to cognition and behavior," says Mosher. "The second goal is to investigate how the heartbeat and breathing, in turn, influences behavior or cognition."

More information: *Cell Reports*, Mosher et al.: "Cellular classes in the human brain revealed in vivo by heartbeat-related modulation of the extracellular action potential waveform" www.cell.com/cell-reports/full … 2211-1247(20)30188-1 , DOI: 10.1016/j.celrep.2020.02.027

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